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Molecular Approaches to Vaccinating Against Hookworm

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Human hookworm infection is a major problem in the developing nations of the tropics, with an estimated one billion infections worldwide. In China alone there are 194 million cases based on a survey comprised of 1,477,742 fecal examinations between 1988-92 (Hotez et al, 1997). Over the last decade, hookworm remains a significant public health problem with high rates of infection throughout southern China, especially *Necator americanus* infections in Hainan (Gandhi et al, 2001), Sichuan (Liu et al, 1999), and Yunnan Provinces, and *Ancylostoma duodenale* infections further north in Anhui and Jiangsu Provinces (Sun et al, 1998; Wang et al, 1999). Conventional approaches to control hookworm that rely on benzimidazole (BZ) anthelmintics have been largely unsuccessful in China and elsewhere in Asia. Their failure is a result of high rates of posttreatment reinfection as well as the concern about emerging BZ drug resistance (Imoisili et al, 2001).

As an alternative approach to control, we have been working on developing a recombinant vaccine against hookworm. We are taking a cocktail vaccine approach that targets both the third stage infective larvae and adult stages of the parasite (Hotez et al, 1999). The larval stage vaccine antigens are targeted to reproduce the immune responses that comprise successful irradiated larval vaccines. These include the cysteine rich secretory proteins (ASP-1 and ASP-2) (Hawdon et al, 1999; Zhan et al, 1999), as well as a secreted metalloprotease known as MTP (Zhan et al, 2001). Vaccination of mice and hamsters with ASP-1 and its peptide derivatives results in greatly lowered worm burdens relative to unvaccinated controls (Ghosh and Hotez, 1999; Liu et al, 2001). Among the adult antigens under evaluation is MEP, the major metalloprotease that lines the parasite alimentary canal (Jones and Hotez, 2001), and secreted protease inhibitors. The vaccines are being evaluated with both conventional and novel adjuvants. Novel platform technologies are also under evaluation.